Title: The association between cardiorespiratory fitness and cardiometabolic risk in children is mediated by abdominal adiposity: the HAPPY study

Running title: Cardiorespiratory fitness and cardiometabolic risk

Manuscript type: Original research

Abstract word count: 188

Manuscript word count: 4,456

Date of submission: 8th September 2014

Abstract

Background: It is unclear whether cardiorespiratory fitness (CRF) is independently linked to cardiometabolic risk in children. This study investigated a) the association between CRF level and presence of cardiometabolic risk disorders using health-related cut points, and b) whether these associations were mediated by abdominal adiposity in children. **Methods:** This was a cross-sectional design study. Anthropometry, biochemical parameters and CRF were assessed in 147 schoolchildren (75 girls) aged 10-14 years. CRF was determined using a maximal cycle ergometer test. Children were classified as 'fit' or 'unfit' according to published thresholds. Logistic regression was used to investigate the odds of having individual and clustered cardiometabolic risk factors according to CRF level and whether abdominal adiposity mediated these associations. **Results:** Children classified as unfit had increased odds of presenting individual and clustered cardiometabolic risk factors ($p < 0.05$), but these associations no longer remained after adjusting for abdominal adiposity ($p > 0.05$). **Conclusions:** This study suggests that the association between CRF and cardiometabolic risk is mediated by abdominal adiposity in 10-14 year-old children and that abdominal adiposity may be a more important determinant of adverse cardiometabolic health in this age group.

Introduction

Cardiovascular disease (CVD) and Type 2 diabetes mellitus (T2DM)-related morbidity and mortality is a significant health and economic burden worldwide[1]. The International Diabetes Federation (IDF) defines the metabolic syndrome as the presence of abdominal obesity (high waist circumference) plus at least two of the following risk factors: high triglycerides, low high-density lipoprotein-cholesterol (HDL), raised blood pressure (BP), and impaired fasting glucose[2]. Each of these is an independent risk factor for CVD and T2DM in adults[3] and clustering of these risk factors may confer additive risk beyond the level predicted by individual components[4]. Risk factor clustering is reported in children and tracks through to adulthood [5]. Early detection of adverse cardiometabolic risk profiles would thus be beneficial and allow early identification of individuals who may benefit from interventions to prevent future morbidity.

A growing body of literature demonstrates an adverse relationship between low cardiorespiratory fitness (CRF) and cardiometabolic risk in children[6-9]. CRF has been independently linked to singular and clustered cardiometabolic risk variables in children[6, 7, 10, 11], but evidence in adults suggests that high CRF may be protective of adverse cardiometabolic health outcomes irrespective of weight status[12]. In the European Youth Heart Study, adjusting for waist circumference attenuated the relationship between CRF and cardiometabolic risk in 9-10 and 15-16 year-old children[13], while Jago et al[14] reported that the effects of change in fitness on individual risk factors were negligible once change in body mass had been accounted for in 6 and 9 year-old children. Ruiz et al[7] reported receiver operating characteristic (ROC)-generated thresholds for CRF related to metabolic risk in 9-10 year-olds and subsequent research supports their use in identifying children and adolescents with increased clustered cardiometabolic risk[6]. However, any potential interaction effects between CRF and adiposity on cardiometabolic risk were not explored and the appropriateness of health-related CRF thresholds in children remains questionable. The interaction of CRF and adiposity on cardiometabolic risk in children remains poorly understood and further exploration is required.

This study therefore investigates a) the association between CRF level and presence of cardiometabolic risk disorders using health-related cut points, and b) whether these associations are mediated by abdominal adiposity in 10-14 year-old children. It was hypothesised that CRF would be favourably associated with cardiometabolic risk but that these associations would be attenuated by adiposity.

Materials and methods

Subjects

The 147 participants (75 girls) included were part of the Health And Physical activity Promotion in Youth (HAPPY) study. This school-based study explored the effects of three interventions on physical activity levels and health outcomes in 10-14 year-old schoolchildren. This secondary school age group was selected as reductions in physical activity levels are evident during the transition from primary to secondary school[15] and identification of effective interventions to tackle this issue are thus warranted. Participants were recruited on a voluntary basis in 11 middle and upper schools across Bedfordshire, UK, and those with complete baseline data were investigated in the present study. Participants were excluded if they were on medication for high blood pressure or if they had heart conditions, dizziness, or joint pain that could be exacerbated through exercise. The study was approved by the University of Bedfordshire ethics review board and conformed to the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from participants' parents and verbal assent from the participants before any testing procedures. Part of the consent form gave parents the option to remove their child from the blood sampling procedure and this resulted in exclusion of 93 participants from the current analysis.

Measurements

Stature and waist circumference (at the umbilicus) were recorded to the nearest 0.5 cm using the portable Leicester Height Measure (Seca, Birmingham, UK) and an adjustable tape measure (Hoechstmass, Sulzbach, Germany), respectively. Body mass and body fat% were recorded to the nearest 0.1 kg and 0.1%, respectively, using the Tanita BC-418 Segmental Body Composition Analyzer (Tanita Corp., Tokyo, Japan). Body mass index (BMI) was calculated using the equation: BMI = body mass (kg) ÷ stature^2 (m^2). UK 1990 reference values were used to calculate *z*-scores for height, weight, and BMI[16, 17] and McCarthy et al[18] reference values used to calculate *z*-scores for waist circumference (*z*-WC). Ethnicity was recorded as white or non-white.

Sitting BP was measured (Omron M5-I automated oscillatory device, Omron Matsusaka Co. Ltd., Matsusaka, Japan) after the participant had rested for 5 min. Three BP readings were obtained and the average of the lowest two readings recorded. Following an overnight fast, 40 µl blood samples were obtained using a finger prick method and analysed using a Cholestech LDX analyser (Cholestech Corp., Hayward, CA.) to provide a valid measure of total cholesterol (TC), HDL, non-HDL, triglycerides, and blood glucose levels[19]. Participants were required to have fasted from 9 pm the night before measurements were performed. Body composition and blood measurements were taken between 8-10 am and participants were instructed to bring a snack with them to eat for breakfast subsequently.

CRF was determined indirectly using a previously validated age- and sex-specific all-out progressive cycle ergometer test to exhaustion[20] and this took place a minimum of 90 min after the breakfast snack. Workloads increased every 3 min until the participant was no longer able to continue. A maximal effort was deemed as a final heart rate ≥ 185 bpm and subjective observation from the researcher that the child could not continue. Power output (watts) was calculated as being equal to $W_1 + (W_2 \cdot t/180)$, where W_1 is work rate at fully completed stage, W_2 is the work rate increment at final incomplete stage, and t is time in seconds at final incomplete stage. VO_{2max} was calculated using previously described formulae[7] and expressed as mL per kilogram of body mass per min (mL/kg/min). Eight participants did not achieve a maximal effort and were excluded from the analysis.

Abdominal obesity was defined as a waist circumference ≥ 90th percentile for age and sex according to McCarthy et al[18]. Hypercholesterolaemia was defined as TC ≥ 5.17 mmol/L[21]. The National Cholesterol Education Program's (NCEP) Pediatric Panel Report[21] gives a range of 0.91-1.16 mmol/L for borderline low HDL levels and 1.02-1.46 mmol/L for borderline high triglyceride concentrations for all sexes and ages. Therefore, the midpoint of these ranges was used as the 10th percentile value to define low HDL (≤ 1.03 mmol/L) and the 90th percentile value to define high triglyceride concentrations (≥ 1.24 mmol/L). A high non-HDL level was defined as ≥ 3.1 mmol/L[22]. Impaired fasting glucose was defined as ≥ 5.6 mmol/L according to the IDF recommendation for children and adolescents[2]. High systolic and diastolic BP were defined as ≥ 90th percentile for age, sex, and height based on published reference values[23]. Metabolic syndrome was defined as having ≥ 3 of the following cardiometabolic risk factors: abdominal obesity, low HDL, hypertriglyceridemia, high systolic or diastolic BP, and impaired fasting glucose. CRF values > 37.0 mL/kg/min for girls and > 42.1 mL/kg/min for boys represented a high CRF level, while values below these levels represented low CRF[7]. These cut points were selected as they have previously been used to identify increased clustered cardiometabolic risk in children[6, 7].

TC:HDL ratio and triglycerides were non-normally distributed and were log-transformed. A continuous clustered cardiometabolic risk variable was then constructed by standardising (to the mean by sex) and then summing the *z*-scores of the following continuously distributed variables that were obtained in the HAPPY study and are linked to increased risk of cardiometabolic disease[3]: diastolic BP, blood glucose, TC:HDL ratio, and fasting triglycerides. Adiposity was not included in this clustered risk score as it would have confounded the results of the data analysis. Participants were then assigned to a 'normal' or 'at-risk' clustered cardiometabolic

risk group according to sex, with high risk defined as ≥1 SD in risk score above the pooled mean. This method has been used previously in similar aged children[24, 25].

Statistical analysis

Analyses were completed using SPSS version 19.0 (SPSS Inc., Chicago, IL.). Odds ratios (ORs) and 95% confidence intervals (CI) for having individual and clustered cardiometabolic risk disorders according to CRF level were explored using logistic regression after controlling for age, sex and ethnicity (model 1). To explore if CRF was independently associated with cardiometabolic risk, these regression models were additionally adjusted for *z*-WC (model 2). Lastly, a logistic regression model that included CRF level and abdominal obesity (high *z*-WC) status as independent variables with the clustered cardiometabolic risk score as the outcome measure was performed, controlling for age, sex, and ethnicity. The level of significance was set at $p < 0.05$.

Results

Descriptive characteristics of the sample can be seen in Table 1. According to body fat%, 4.8% of the sample were obese, 12.9% were overfat, and 82.3% were normal[26]. Abdominal obesity (high *z*-WC) was prevalent in 16.3% of the sample, hypercholesterolemia in 5.4%, low HDL in 12.2%, high non-HDL in 18.4%, hypertriglyceridaemia in 16.3%, impaired fasting glucose in 16.3%, high systolic BP in 15.6%, and high diastolic BP in 15.6%. Low CRF was prevalent in 36.1% of the sample. 12.2% of the sample were defined as having the metabolic syndrome and 15.0% had a high clustered cardiometabolic risk score.

Multivariate adjusted ORs (and 95% CIs) for having adverse cardiometabolic risk factor levels across CRF groups are presented in Table 2. When adjusting for age, sex, and ethnicity, the odds of having abdominal obesity were substantially higher in children with low CRF (OR = 64.37; 95% CI 8.11, 510.84, p <0.01) compared to their fit counterparts. Children with low CRF also had higher odds of having high non-HDL, hypertriglyceridemia, elevated diastolic BP, the metabolic syndrome, and increased clustered cardiometabolic risk score (see Table 2). When further adjusting for *z*-WC, the associations between CRF and cardiometabolic risk variables weakened and no significant associations were observed (Table 2).

When ORs and 95% CIs were calculated for having an increased clustered cardiometabolic risk with CRF level and *z*-WC category entered as independent variables (after controlling for age, sex, and ethnicity), the odds were significantly higher in children with abdominal obesity compared to those who were non-obese (OR

146 = 5.83; 95% CI 1.49, 22.81, p = 0.01), while there was no significant difference in odds between children with
147 high versus low CRF (1.25; 0.34, 4.63, p = 0.74).
148
149 **Discussion**
150 The primary finding of this study was that the association between CRF and cardiometabolic risk in children
151 was mediated by abdominal adiposity. As such, after adjusting for age, sex, ethnicity, and abdominal adiposity,
152 CRF was not independently associated with any individual or clustered cardiometabolic risk variable. It thus
153 appears that in this sample of children, the association between CRF and cardiometabolic risk is a function of
154 abdominal adiposity.
155 In the regression models that did not adjust for abdominal adiposity in this current study, unfit children
156 had increased odds of having high non-HDL cholesterol, hypertriglyceridemia, elevated diastolic BP, and the
157 metabolic syndrome compared to fit children when classified using previously published health-related CRF
158 thresholds. The odds of having an increased composite cardiometabolic risk score were also higher in unfit
159 children. Previous studies have reported similar findings when not adjusting for adiposity and support the use of
160 CRF as a risk stratification tool to identify children at increased risk of cardiometabolic disease[10, 13, 27]. However,
161 when adjusting for abdominal adiposity, low CRF was not associated with the presence of any individual risk
162 factor or an increased clustered risk score in this current study, which may not be surprising given the
163 exceptionally high odds ratio for having abdominal obesity in children with low CRF (OR = 64.37). This current
164 data suggests that the relationship between CRF and cardiometabolic risk in children may be mediated via
165 abdominal adiposity.
166 Several studies have documented attenuated relationships between CRF and individual cardiometabolic
167 risk factors following adjustment for adiposity[28-30]. Nonetheless, exploring associations with a clustered risk
168 score is now considered preferable in pediatric populations for reasons cited previously[6, 10, 31], which include
169 improved representation of the constellation of disturbances associated with cardiometabolic disease and
170 reduced sensitivity to daily changes in individual risk markers. Recent evidence supports the findings of the
171 current study whereby associations between CRF and clustered risk scores did not remain significant in children
172 after adjusting for adiposity[27, 32]. This is despite differences in methods used to determine CRF and construct
173 and define clustered risk scores. For example, Buchan et al[32] constructed a clustered risk score from TC:HDL
174 ratio, triglycerides, the homeostasis model assessment (HOMA), systolic BP, C-reactive protein, interleukin-6,
175 and adiponectin, while Christodoulos et al[27] constructed a score from HDL, the average of combined systolic

and diastolic BP, and glucose, and both studies assessed CRF using a 20 m multi-stage fitness test compared to the maximal incremental cycle ergometer test used in the current study.

As abdominal obesity appears to play a mediating role in the link between CRF and cardiometabolic risk[27, 32], this might suggest that it is the centrally obese children who have the lowest CRF levels and this may be driving the associations observed between CRF and cardiometabolic risk. In the current study, 95.8% of children with abdominal obesity had low CRF, but 24.4% of children without abdominal obesity also had low CRF levels (data not shown). Alternatively, abdominal obesity may be part of the causal pathway between CRF and cardiometabolic risk, in which case, adjusting for this variable will diminish a true association between the latter two[13]. Christodoulos et al[27] argue that even if the association between CRF and cardiometabolic risk disappears after adjusting for a mediating variable, CRF remains the principal cause, which thus may confirm its appropriateness for identifying children at risk of future disease. The potential importance of CRF in children is highlighted by observations that exercise-related enhancement of CRF can improve insulin sensitivity in overweight girls without changes in body composition[33], while changes in CRF from age 13 to 27 years were correlated with changes in TC:HDL ratio after correcting for adiposity[34].

Unfortunately, there is limited longitudinal and randomised control trial data available concerning the relationship between CRF, adiposity, and cardiometabolic risk in children. Jago et al[14] reported findings from 3,514 adolescents that revealed the effects changes in CRF had over a 2-year period on clustered cardiometabolic risk were negligible once changes in body mass had been taken into account. In adults, however, an interaction effect between adiposity and CRF is recognised with high levels of CRF protecting against adverse health outcomes in overweight males[35]. These data may suggest that maintaining a healthy body weight is more important in children, while in adults, health improvement strategies should focus on CRF. This concept is supported by evidence that associations between adiposity and clustered cardiometabolic risk in children declines with age, while the association between CRF and cardiometabolic risk strengthens[36]. This changing relationship may be due to sexual maturation[36]. In the current sample of 10-14 year-olds, abdominal obesity was independently associated with increased clustered cardiometabolic risk, while this was not apparent for CRF. It is a priority to understand the roles that CRF and adiposity play at different stages of the lifecourse to effectively target preventative health interventions.

Limitations of the current study include the cross-sectional design and small sample size. A maximal effort was required in the CRF test and may not be suitable for individuals with clinical pathology, although this is likely to account for only a small number of children. It is possible the strength of associations between

cardiometabolic risk and CRF may differ when employing alternative proposed health-related thresholds. However, it is unknown which cardiometabolic risk thresholds, e.g. low HDL or impaired fasting glucose, present the greatest risk for future adverse health outcomes. This study was unable to adjust for biological maturity status as no measure was available. Although the analyses accounted for age-related changes in the cardiometabolic risk variables, these variables are influenced by puberty[37]. Biological maturity thus represents a major confounding variable that could not be accounted for. Other factors that may confound the association between CRF, adiposity, and cardiometabolic risk, such as dietary intake, presence of Type 1 or Type 2 diabetes, smoking status, or use of lipid lowering drugs or corticosteroids were not accounted for and should be considered in future research.

In conclusion, this study suggests that the association between CRF and cardiometabolic risk in 10-14 year-old children is mediated by abdominal adiposity and that abdominal adiposity may be a more important determinant of adverse cardiometabolic health in this age group. More data is required to better understand the roles that fitness and fatness play in determining health risk in young populations but it may be feasible to recommend lifelong health improvement strategies that focus on improving CRF and preventing excess weight gain.

Acknowledgements

The authors would like to thank the participants who gave their time to the study. We would also like to thank all of the schools who helped facilitate the research.

Funding source

This study was funded by the Bedford Charity (grant number 166/308).

228 **References**

229 1. Kelly BB, Narula J, Fuster V. Recognizing global burden of cardiovascular disease and related chronic
230 diseases. *Mt Sinai J Med*. 2012;79:632-640.

231 2. Zimmet P, Alberti KG, Kaufman F, et al. The metabolic syndrome in children and adolescents - an IDF
232 consensus report. *Pediatr Diabetes*. 2007;8:299-306.

233 3. Graham I, Atar D, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in
234 clinical practice: executive summary: Fourth Joint Task Force of the European Society of Cardiology and Other
235 Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J*. 2007;28:2375-2414.

236 4. Golden SH, Folsom AR, Coresh J, et al. Risk factor groupings related to insulin resistance and their
237 synergistic effects on subclinical atherosclerosis: the atherosclerosis risk in communities study. *Diabetes*.
238 2002;51:3069-3076.

239 5. Camhi SM, Katzmarzyk PT. Tracking of cardiometabolic risk factor clustering from childhood to adulthood.
240 *Int J Pediatr Obes*. 2010;5:122-129.

241 6. Bailey DP, Boddy LM, Savory LA, et al. Associations between cardiorespiratory fitness, physical activity and
242 clustered cardiometabolic risk in children and adolescents: the HAPPY study. *Eur J Pediatr*. 2012;171:1317-
243 1323.

244 7. Ruiz JR, Ortega FB, Rizzo NS, et al. High cardiovascular fitness is associated with low metabolic risk score
245 in children: the European Youth Heart Study. *Pediatr Res*. 2007;61:350-355.

246 8. Twisk JW, Kemper HC, van Mechelen W. The relationship between physical fitness and physical activity
247 during adolescence and cardiovascular disease risk factors at adult age. The Amsterdam Growth and Health
248 Longitudinal Study. *Int J Sports Med*. 2002;23:S8-14.

249 9. Jago R, Froberg K, Cooper AR, et al. Three-year changes in fitness and adiposity are independently
250 associated with cardiovascular risk factors among young Danish children. *J Phys Act Health*. 2010;7:37-44.

10. Houston EL, Baker JS, Buchan DS, et al. Cardiorespiratory fitness predicts clustered cardiometabolic risk in 10-11.9-year-olds. *Eur J Pediatr*. 2013.

11. Anderssen SA, Cooper AR, Riddoch C, et al. Low cardiorespiratory fitness is a strong predictor for clustering of cardiovascular disease risk factors in children independent of country, age and sex. *Eur Society Cardio*. 2007;14:526-531.

12. McAuley PA, Sui X, Church TS, et al. The joint effects of cardiorespiratory fitness and adiposity on mortality risk in men with hypertension. *Am J Hypertens*. 2009;22:1062-1069.

13. Ekelund U, Anderssen SA, Froberg K, et al. Independent associations of physical activity and cardiorespiratory fitness with metabolic risk factors in children: the European Youth Heart Study. *Diabetologia*. 2007;50:1832-1840.

14. Jago R, Drews KL, McMurray RG, et al. BMI change, fitness change and cardiometabolic risk factors among 8th grade youth. *Pediatr Exerc Sci*. 2013;25:52-68.

15. Cooper AR, Jago R, Southward EF, et al. Active travel and physical activity across the school transition: the PEACH project. *Med Sci Sports Exerc*. 2012;44:1890-1897.

16. Freeman JV, Cole TJ, Chinn S, et al. Cross sectional stature and weight reference curves for the UK, 1990. *Arch Dis Child*. 1995;73:17-24.

17. Cole TJ, Freeman JV, Preece MA. Body mass index reference curves for the UK, 1990. *Arch Dis Child*. 1995;73:25-29.

18. McCarthy HD, Jarrett KV, Crawley HF. The development of waist circumference percentiles in British children aged 5.0-16.9 y. *Eur J Clin Nutr*. 2001;55:902-907.

19. Parikh P, Mochari H, Mosca L. Clinical utility of a fingerstick technology to identify individuals with abnormal blood lipids and high-sensitivity C-reactive protein levels. *Am J Health Promot*. 2009;23:279-282.

20. Riddoch C, Edwards D, Page A, et al. The European Youth Heart Study - cardiovascular disease risk factors in children: rationale, aims, study design, and validation of methods. *J Phys Act Health*. 2005;2:115-129.

21. National Cholesterol Education Panel. Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. Bethesda, Md: National Institute of Health, 1991. NIH Publication No. 91-2732. 1991.

22. Li C, Ford ES, McBride PE, et al. Non-high-density lipoprotein cholesterol concentration is associated with the metabolic syndrome among US youth aged 12-19 years. *J Pediatr*. 2011;158:201-207.

23. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents: a working group report from the National High Blood Pressure Education Program. *Pediatrics*. 1996;98:649-658.

24. Andersen LB, Harro M, Sardinha LB, et al. Physical activity and clustered cardiovascular risk in children: a cross-sectional study (The European Youth Heart Study). *Lancet*. 2006;368:299-304.

25. Gobbi RM, Davies IG, Fairclough SJ, et al. Clustered cardiometabolic risk, cardiorespiratory fitness and physical activity in 10-11 year old children. The CHANGE! Project Baseline. *Arch Exerc Health Dis*. 2012;3:207-213.

26. McCarthy HD, Cole TJ, Fry T, et al. Body fat reference curves for children. *Int J Obes (Lond)*. 2006;30:598-602.

27. Christodoulos AD, Douda HT, Tokmakidis SP. Cardiorespiratory fitness, metabolic risk, and inflammation in children. *Int J Pediatr*. 2012;2012:270515.

28. Boreham C, Twisk J, Murray L, et al. Fitness, fatness, and coronary heart disease risk in adolescents: the Northern Ireland Young Hearts Project. *Med Sci Sports Exerc*. 2001;33:270-274.

29. Martinez-Gomez D, Eisenmann JC, Warnberg J, et al. Associations of physical activity, cardiorespiratory fitness and fatness with low-grade inflammation in adolescents: the AFINOS Study. *Int J Obes (Lond)*. 2010;34:1501-1507.

296 30. Shaibi GQ, Cruz ML, Ball GD, et al. Cardiovascular fitness and the metabolic syndrome in overweight
297 Latino youths. *Med Sci Sports Exerc*. 2005;37:922-928.

298 31. Steele RM, Brage S, Corder K, et al. Physical activity, cardiorespiratory fitness, and the metabolic syndrome
299 in youth. *J Appl Physiol*. 2008;105:342-351.

300 32. Buchan DS, Young JD, Boddy LM, et al. Independent associations between cardiorespiratory fitness, waist
301 circumference, BMI, and clustered cardiometabolic risk in adolescents. *Am J Hum Biol*. 2014;26:29-35.

302 33. Nassis GP, Papantakou K, Skenderi K, et al. Aerobic exercise training improves insulin sensitivity without
303 changes in body weight, body fat, adiponectin, and inflammatory markers in overweight and obese girls.
304 *Metabolism*. 2005;54:1472-1479.

305 34. Twisk JW, Kemper HC, van Mechelen W. Tracking of activity and fitness and the relationship with
306 cardiovascular disease risk factors. *Med Sci Sports Exerc*. 2000;32:1455-1461.

307 35. Lee CD, Blair SN, Jackson AS. Cardiorespiratory fitness, body composition, and all-cause and
308 cardiovascular disease mortality in men. *Am J Clin Nutr*. 1999;69:373-380.

309 36. Ondrak KS, McMurray RG, Bangdiwala SI, et al. Influence of aerobic power and percent body fat on
310 cardiovascular disease risk in youth. *J Adolesc Health*. 2007;41:146-152.

311 37. Hannon TS, Janosky J, Arslanian SA. Longitudinal study of physiologic insulin resistance and metabolic
312 changes of puberty. *Pediatr Res*. 2006;60:759-763.

313

314

315 **Table 1** Descriptive characteristics of participants

Variable	All (*n* = 147)	Boys (*n* = 72)	Girls (*n* = 75)
Age (years)	11.80 (1.35)	11.97 (1.38)	11.63 (1.30)
z-height	0.32 (1.10)	0.33 (1.19)	0.31 (1.00)
z-weight	0.26 (1.63)	0.03 (1.22)	0.48 (1.94)
z-BMI	-0.27 (1.38)	-0.32 (1.21)	-0.23 (1.53)
Body fat%	20.4 (6.3)	17.2 (5.4)	23.4 (5.6)
z-waist circumference	0.25 (1.45)	-0.02 (1.27)	0.51 (1.58)
Systolic BP (mm Hg)	109.2 (9.6)	110.6 (9.8)	107.8 (9.2)
Diastolic BP (mm Hg)	68.6 (7.0)	68.4 (7.5)	68.7 (6.5)
Total cholesterol (mmol/L)	3.92 (0.68)	3.81 (0.68)	4.02 (0.66)
HDL (mmol/L)	1.44 (0.38)	1.43 (0.39)	1.44 (0.37)
TC:HDL ratio	2.93 (1.03)	2.86 (1.03)	2.99 (1.03)
Triglycerides (mmol/L)	0.86 (0.57)	0.77 (0.40)	0.93 (0.69)
Blood glucose (mmol/L)	5.08 (0.50)	5.09 (0.50)	5.07 (0.50)
VO_{2max} (mL/kg/min)	42.47 (9.68)	46.58 (8.60)	38.52 (9.03)

316 Data presented as mean (SD). *z*-BMI, body mass index *z*-score; BP, blood pressure; HDL, high-density

317 lipoprotein cholesterol; TC, total cholesterol.

318 **Table 2** Multivariate-adjusted odds ratios (and 95% CIs) for cardiometabolic risk factors according to cardiorespiratory fitness status (high cardiorespiratory fitness =
319 reference group)

	Model 1		*Model 2*	
Risk factor	Odds ratio (95% CI)	*p* value	Odds ratio (95% CI)	*p* value
Hypercholesterolaemia[1] (*n* = 8)	2.28 (0.46, 11.34)	0.32	2.04 (0.34, 12.36)	0.44
Low HDL[2] (*n* = 18)	1.32 (0.45, 3.83)	0.61	0.77 (0.20, 2.96)	0.70
High non-HDL[3] (*n* = 27)	3.45 (1.36, 8.74)	<0.01	2.68 (0.90, 8.03)	0.08
Hypertriglyceridemia[4] (*n* = 24)	3.37 (1.26, 9.04)	0.02	2.08 (0.64, 6.72)	0.22
Impaired fasting glucose[5] (*n* = 24)	1.22 (0.47, 3.17)	0.69	0.97 (0.30, 3.11)	0.96
Elevated systolic BP[7] (*n* = 23)	1.11 (0.41, 3.04)	0.84	0.65 (0.18, 2.33)	0.50
Elevated diastolic BP[7] (*n* = 23)	2.77 (1.01, 7.60)	0.04	1.84 (0.55, 6.12	0.32
Metabolic syndrome[8] (*n* = 18)	5.45 (1.71, 17.43)	<0.01	1.12 (0.24, 5.35)	0.89
Increased clustered risk[9] (*n* = 22)	7.63 (2.41, 24.21)	<0.01	1.40 (0.40, 4.90)	0.60

320 Model 1, adjusted for age, sex and ethnicity; Model 2, additionally adjusting for abdominal adiposity. HDL, high-density lipoprotein cholesterol; BP, blood pressure; [1]≥ 5.17
321 mmol/L; [2]≤ 1.03 mmol/L; [3]≥ 3.14 mmol/L; [4]≥ 1.24 mmol/L; [5]≥ 5.6 mmol/L; [6]≥ 90th percentile for age and sex; [7]≥ 90th percentile for age, sex and height; [8]≥ 3 risk factors;
322 [9]clustered risk score ≥ 2.93.

323